group or a cyano-lower alkenyl group, and the chains of R^{16} optionally contain a hetero atom, when Z is a group represented by the formula (Z_1), R16 is a substituted or optionally substituted aryl or heteroaryl group, and m represents an integer of 0 to 5.

A9 Cont

REMARKS

The specification and Claim 1 have been amended in order to rectify several readily apparent typographical errors. The changes and support therefor are listed below.

(1) A proviso reading "when E represents cyclopentyl group, cyclohexyl group, pyrrolidinone-1-yl group or piperidinone-1-yl group, Z is a group represented by the formula (Z_2)" was added to the definition of E in formula (1) in claim 1.

(2) A proviso reading "when Z is a group represented by formula (Z_1), R16 is a substituted or unsubstituted aryl group or a substituted or unsubstituted heteroaryl group" was added to the definition of Z in formula (1) in claim 1.

(3) The compound name in Example 58 appearing at page 84, lines 16 to 18 was changed to "4-(3-chlorophenyl)-6-methyl-2-methylsulfanyl-1,4- dihydropyrimidine-5-carboxylic acid (3-phenyl-2 -propene-1-yl)amide".

This correct compound name is evident from the fact that "3-acetyl-3-(3-chlorophenyl)-N-(3-phenyl-2-propene-1-yl)acrylamide" was used as the starting material appearing at page 86, lines 4 to 5 and also from the chemical structural formula in Table 1 (Example 58) on page 104. This compound name is clearly supported by the specification.

(4) The compound name appearing on page 86, lines 2 to 3 was changed to "4-(3-chlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3-phenyl-2-propene-1-yl)amide".

This correct compound name is evident from the fact that "3-acetyl-3-(3-5 chlorophenyl)-N-(3-phenyl-2-propene-1-yl)acrylamide" was used as the starting material appearing on page 86, lines 4-5 and also from the chemical structural formula in Table 1 on page 104 . This compound name does not exceed the range of the disclosure at the time of the international application.

(5) The compound name in Example 59 appearing on (page 86, lines 20 to 21 was changed to "4-(3-chlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3,3-diphenylpropyl)amide".

This correct compound name is evident from the facts that the compound of Example 59 was synthesized in the same manner as that in Example 58 and also that 3-acetyl-3-(3-chlorophenyl)-N-(3,3-diphenylpropyl)acrylamide was used as the starting material for this compound appearing on page 84, line 18 to page 86, line 1. This compound name is apparent also from Table 1 (Example 59) on page 104. This compound name is clearly supported by the present specification.

(6) The compound name in Example 66 appearing on page 90 lines 10 to 11 was changed to "4-(3-chlorophenyl)-6-methyl-2-(pyridine-3-yl)-1,4-dihydropyrimidine-5-carboxylic acid (3,3-diphenylpropyl)amide".

This correct compound name is evident from the facts that the compound of Example 66 was synthesized in the same manner as that in Example 58 and also that 3-acetyl-3-(3-chlorophenyl)-N-(3,3-diphenylpropyl)acrylamide was used as the starting material for this compound appearing on page 84, line 18 to page 86, line 1. This compound name is apparent also from the chemical structural formula in Table 1 (Example 66) on page 105. This compound name is clearly supported by the present specification.

(7) The compound name in Example 67 appearing on page 92, lines 4 to 5 (page 90, lines 18 to 19 of the English translation) was changed to "4-(3-chlorophenyl)-6-methyl-2-phenyl-1,4-dihydropyrimidine-5-carboxylic acid (3,3-diphenylpropyl)amide".

This correct compound name is evident from the facts that the compound of Example 67 was synthesized in the same manner as that in Example 58 and also that 3-acetyl-3-(3-chlorophenyl)-N-(3,3-diphenylpropyl)acrylamide was used as the starting material for this compound appearing on page 84, line 18 to page 86, line 1. This compound name is apparent also from the chemical structural formula in Table 1 (Example 67) on page 105. This compound name is clearly supported by the present specification.

(8) The compound name in Example 79 appearing on page 95, lines 1 to 2 was changed to "4-(3,4-dichlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3-phenylpropyl)amide".

This correct compound name is evident from the facts that the compound of Example 79 was synthesized in the same manner as that in Example 58 and also that 3-acetyl-3-(3,4-dichlorophenyl)-N-(3-3-phenylpropyl)acrylamide was used as the starting material for this compound appearing on page 84, line 18 to page 86, line 1. This compound name is apparent also from the chemical structural formula in Table 1 (Example 79) on page 106 of the English translation. This compound name is clearly supported by the specification.

(9) The compound name in Example 80 appearing on page 95, lines 9 to 10 was changed to "4-(3,4-dichlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3,3-diphenylpropyl)amide".

This compound name is evident from the facts that the compound of Example 80 was synthesized in the same manner as that in Example 58 and also that 3-acetyl-3-(3,4-

dichlorophenyl)-N-(3,3-diphenylpropyl)acrylamide was used as the starting material for this compound appearing on page 84, line 18 to page 86, line 1. This compound name is apparent also from the chemical structural formula in Table 1 (Example 80) on page 106 of the English translation. This compound name is clearly supported by the specification.

(10) The compound name in Example 81 appearing on page 95, lines 17 to 18 was changed to "4-(3,4-dichlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3-phenyl-2 -propene-1-yl)amide".

This correct compound name is evident from the facts that the compound of Example 81 was synthesized in the same manner as that in Example 58 and also that 3-acetyl-3-(3,4-dichlorophenyl)-N-(3-phenyl-2-propene-1-yl)acrylamide was used as the starting material for this compound appearing on page 84, line 18 to page 86, line 1. This compound name is apparent also from the chemical structural formula in Table 1 (Example 81) on page 107. This compound name is clearly supported by the present specification.

It is believed that this application is now in condition for examination on the merits.

Favorable consideration is earnestly solicited.

Respectfully submitted,

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Serial No: 10/025,589
Amendment Filed on: Herewith

IN THE SPECIFICATION

Page 84, lines 16-18, please replace the paragraph with the following paragraph:

--Example 58 Synthesis of [4-(3-chlorophenyl)-2-methylsulfanyl]4-(3-chlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3-phenyl-2-propene-1-yl)amide:

1) Synthesis of 3-oxo-N-(3-phenyl-2-propene-1-yl)butyramide:

Page 86, lines 2-3, please replace the paragraph with the following paragraph:

3) Synthesis of [4-(3-chlorophenyl)-2-methylsulfanyl]4-(3-chlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydro-pyrimidine-5-carboxylic acid (3-phenyl-2-propene-1-yl)amide:

Page 86, lines 20-21, please replace the paragraph with the following paragraph:

Example 59 Synthesis of [4-(3-chlorophenyl)-2-methylsulfanyl] 4-(3-chlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3,3-diphenylpropyl)amide:

Page 90, lines 10-11, please replace the paragraph with the following paragraph:

Example 66 Synthesis of [4-(3-chlorophenyl)]4-(3-chlorophenyl)-6-methyl-2-pyridine-3-yl-1,4-dihydropyrimidine-5-carboxylic acid (3,3-diphenylpropyl)amide:

Page 90, lines 18-19, please replace the paragraph with the following paragraph:

Example 67 Synthesis of [4-(3-chlorophenyl)]4-(3-chlorophenyl)-6-methyl-2-phenyl-1,4-dihydro-pyrimidine-5-carboxylic acid (3,3-diphenylpropyl)amide:

Page 95, lines 1-2, please replace the paragraph with the following paragraph:

Example 79 Synthesis of [4-(3,5-dichlorophenyl)]4-(3,4-dichlorophenyl)-6-methyl-2-

methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3-phenylpropyl)amide:

Page 95, lines 9-10, please replace the paragraph with the following paragraph:

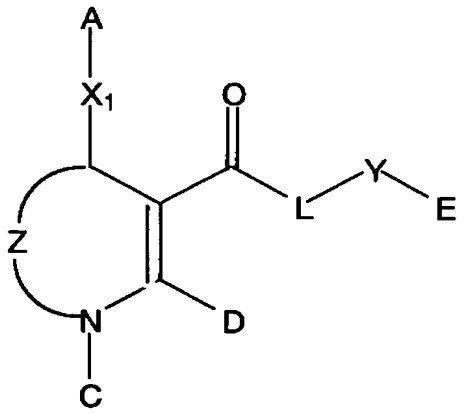
Example 80 Synthesis of [4-(3,4-dichlorophenyl)]4-(3,4-dichlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3,3-diphenylpropyl)amide:

Page 95, lines 17-28, please replace the paragraph with the following paragraph:

Example 81 Synthesis of [4-(3,4-dichlorophenyl)]4-(3,4-dichlorophenyl)-6-methyl-2-methylsulfanyl-1,4-dihydropyrimidine-5-carboxylic acid (3-phenyl-2-propene-1-yl)amide:

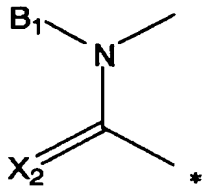
IN THE CLAIMS

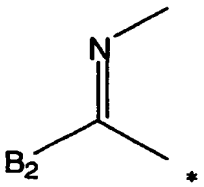
1. (Amended) [Dihydropyrimidine derivatives] A dihydropyrimidine compound of the following [general] formula (1), a [tautomers] tantomer thereof [and] or a pharmaceutically acceptable [salts] salt thereof.



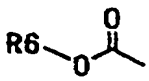
(1)

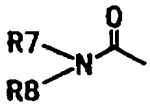
wherein Z represents a group of the following general formula (Z1) or (Z2), which is bonded to the nitrogen atom at a symbol "*".

(Z1) 

(Z2) 

wherein B_1 represents hydrogen atom, a lower alkyl group which [may contain] optionally contains a hetero atom in the chain thereof, a lower alkylcarbonyl group (only when L represents oxygen atom, Y represents an interatomic bond and E represents hydrogen atom), an aryl-lower alkyl group, a heteroaryl-lower alkyl group, a hydroxy-lower alkyl group, a halogeno-lower alkyl group, an amino-lower alkyl group, a carboxy-lower alkyl group, a lower alkyloxycarbonyl-lower alkyl group or a group of the following general formula (3) or (4):

(3) 

(4) 

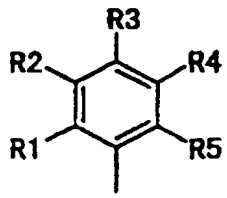
wherein R^6 to R^8 each represent hydrogen atom, a linear, branched or cyclic, saturated or unsaturated hydrocarbon group having 1 to 6 carbon atoms, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, a hydroxy-lower alkyl group, a hydroxy-lower alkenyl group, a halogeno-lower alkyl group, a halogeno-lower alkenyl group, an amino-lower alkyl group, an amino-lower alkenyl group, a carboxy-lower alkyl group, a

carboxy-lower alkenyl group, a substituted or unsubstituted aryl-lower alkyl group, a substituted or unsubstituted aryl-lower alkenyl group, a substituted or unsubstituted diaryl-lower alkyl group, a substituted or unsubstituted heteroaryl-lower alkyl group, a substituted or unsubstituted heteroaryl-lower alkenyl group, a cyano-lower alkyl group or a cyano-lower alkenyl group, and the chains of R^6 to R^8 may contain a hetero atom, with the proviso that when R^6 to R^8 each represent a linear, branched or cyclic, saturated or unsaturated hydrocarbon group having 1 to 6 carbon atoms, a substituted or unsubstituted aryl group, a hydroxy-lower alkyl group, a hydroxy-lower alkenyl group, a halogeno-lower alkyl group, a halogeno-lower alkenyl group, a carboxy-lower alkyl group, a carboxy-lower alkenyl group, a substituted or unsubstituted aryl-lower alkyl group, a substituted or unsubstituted aryl-lower alkenyl group, a substituted or unsubstituted heteroaryl-lower alkyl group or, a substituted or unsubstituted heteroaryl-lower alkenyl group, L must be oxygen atom, Y must be an interatomic bond and E must be hydrogen atom[,];

B_2 represents an amino group, a lower alkyl group which may contain a hetero atom in the chain thereof, a lower alkylamino group, a lower alkylthio group, an aryl-lower alkyl group, a heteroaryl-lower alkyl group, a hydroxy-lower alkyl group, a halogeno-lower alkyl group, a substituted or unsubstituted aryl group or a substituted or unsubstituted heteroaryl group,

X_2 represents oxygen atom or sulfur atom[,];

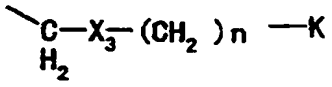
A represents a group of the following general formula (2), or l-naphthyl, 2-naphthyl, indole-2-yl, indole-3-yl, thiophene-3-yl, thiophene-2-yl, furan-3-yl, furan-2-yl, pyridine-4-yl, pyridine-3-yl or pyridine-2-yl group:

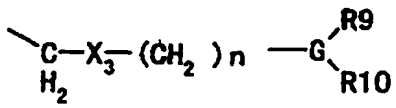
(2) 

wherein R^1, R^2, R^3, R^4 and R^5 may be the same or different from each other and each represent hydrogen atom, a halogen atom, hydroxyl group, carboxyl group, amino group, cyano group, nitro group, a lower alkyl group, a lower alkoxyl group, a lower alkylamino group, a lower alkylthio group, a lower alkanoyl group, a lower alkoxycarbonyl group, a hydroxy-lower alkyl group, a hydroxy-lower alkoxyl group, a hydroxy-lower alkenyl group, a halogeno-lower alkyl group, a halogeno-lower alkoxyl group, an amino-lower alkyl group, an amino-lower alkoxyl group, an amino-lower alkenyl group, a carboxy-lower alkyl group, a carboxy-lower alkoxyl group, a carboxy-lower alkenyl group, an aryl-lower alkoxyl group or an aroyl group[,];

C represents hydrogen atom, a lower alkyl group, a hydroxy-lower alkyl group, an aryl-lower alkyl group, a heteroaryl-lower alkyl group, an amino-lower alkyl group or a carboxy-lower alkyl group[,];

D represents hydrogen atom, a lower alkyl group, dimethoxymethyl group, cyano group, an aryl-lower alkyl group, a heteroaryl-lower alkyl group, a hydroxy-lower alkyl group, a halogeno-lower alkyl group, an amino-lower alkyl group, a carboxy-lower alkyl group or a group of the following general formula (5) or (6):

(5) 

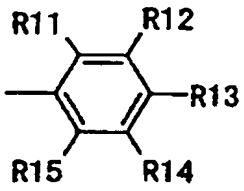
(6) 

wherein X_3 represents O, S or N-R_8', n represents an integer of 0 to 6, K in general formula (5) represents hydrogen atom, a halogen atom, hydroxyl group, carboxyl group, amino group, cyano group, nitro group, azido group, a substituted or unsubstituted aryl group or a substituted or unsubstituted heteroaryl group, G in the general formula (6) represents N or C-H, wherein $R^{8'}$ to R^{10} may be the same or different from each other, and they each represent hydrogen atom, a linear, branched or cyclic, saturated or unsaturated hydrocarbon group having 1 to 6 carbon atoms, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, a hydroxy-lower alkyl group, a hydroxy-lower alkenyl group, a halogeno-lower alkyl group, a halogeno-lower alkenyl group, an amino-lower alkyl group, an amino-lower alkenyl group, a carboxy-lower alkyl group, a carboxy-lower alkenyl group, an aryl-lower alkyl group, an aryl-lower alkenyl group, a heteroaryl-lower alkyl group, a heteroaryl-lower alkenyl group, a cyano-lower alkyl group or a cyano-lower alkenyl group, and the chains may contain a hetero atom, or R^9 and R^{10} may together form a ring which may contain a hetero atom[,];

E represents hydrogen atom (only when L represents oxygen atom and Y represents an interatomic bond), a group of the following general formula (7), a substituted or unsubstituted heteroaryl group, cyclopentyl group, cyclohexyl group, pyrrolidinone-1-yl group or piperidinone-1-yl group[:], when E represents cyclopentyl group, cyclohexyl group, pyrrolidinone-1-yl group or piperidinone-1-yl group, Z is a group represented by the formula

(Z_2):

(7)



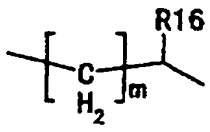
wherein R^{11}, R^{12}, R^{13}, R^{14} and R^{15} may be the same or different from each other and each represent hydrogen atom, a halogen atom, hydroxyl group, carboxyl group, amino group, cyano group, nitro group, a lower alkyl group, a lower alkoxyl group, a lower alkylamino group, a lower alkylthio group, a lower alkanoyl group, a hydroxy-lower alkyl group, a hydroxy-lower alkoxyl group, a hydroxy-lower alkenyl group, a halogeno-lower alkyl group, a halogeno-lower alkoxyl group, an amino-lower alkyl group, an amino-lower alkoxyl group, an amino-lower alkenyl group, a carboxy-lower alkyl group, a carboxy-lower alkoxyl group, a carboxy-lower alkenyl group, an aryl-lower alkyl group, an aryl-lower alkoxyl group, a lower alkoxycarbonyl group, an aroyl group, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group or a saturated cyclic hydrocarbon having 3 to 8 carbon atoms, which may contain a hetero atom in the chain thereof and/or in the ring thereof,

X_1 represents an interatomic bond, $-CH_2-$, $-CH_2CH_2-$, -CH=CH- or -CC-,

L represents >N-F or oxygen atom (only when Z represents Z_1),

wherein F represents hydrogen atom or a lower alkyl group which may contain a hetero atom in the chain thereof, a hydroxy-lower alkyl group, an amino-lower alkyl group, a carboxy-lower alkyl group or a lower alkyloxycarbonyl-lower alkyl group,

Y represents an interatomic bond (only when L represents oxygen atom and E represents hydrogen atom), a saturated or unsaturated linear hydrocarbon group having 1 to 6 carbon atoms, which may contain a hetero atom in the group thereof, or a group of the following general formula (8):

(8) 

wherein R_{16} represents hydrogen atom, a substituted or unsubstituted, saturated or unsaturated linear, branched or cyclic hydrocarbon group having 1 to 6 carbon atoms, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, a hydroxy-lower alkyl group, a hydroxy-lower alkenyl group, a halogeno-lower alkyl group, a halogeno-lower alkenyl group, an amino-lower alkyl group, an amino-lower alkenyl group, a carboxy-lower alkyl group, a carboxy-lower alkenyl group, an aryl-lower alkyl group, an aryl-lower alkenyl group, a heteroaryl-lower alkyl group, a heteroaryl-lower alkenyl group, a cyano-lower alkyl group or a cyano-lower alkenyl group, and the chains of R16 may contain a hetero atom, when Z is a group represented by the formula (Z_1), R16 is a substituted or optionally substituted aryl or heteroaryl group and m represents an integer of 0 to 5.--